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Case Report Open Access

Iatrogenic Delirium in an Elderly Patient: When Drugs are Harmful

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Abstract

Delirium is a global disorder of cognition that represents a medical emergency and, particularly in elderly, is often unrecognized or misdiagnosed and commonly mistaken for dementia, depression, mania, or an acute schizophrenic reaction. Drug-induced delirium is a common matter in the elderly and in this paper we report the onset of delirium induced by drug-drug interaction in a previously health elderly patient.

Keywords: Elderly; Delirium; Drug drug interactions; SSRI; Opiate

Introduction

Delirium or acute confusional state is a transient global disorder of cognition representing a medical emergency related with increased morbidity and mortality rates [1,2].

In the elderly, the onset of delirium represents a prognostic negative factor on morbidity, mortality, functional and cognitive outcomes, and it may run a more chronic course [3].

Delirium is often unrecognized or misdiagnosed and is commonly mistaken for dementia, depression, mania, or an acute schizophrenic reaction, or part of old age, while early diagnosis and resolution of symptoms are correlated with the most favourable outcomes.

Drug-induced delirium is a common matter in the elderly and previously we have reported that anticholinergic drugs, together with several drugs, may significantly contribute to the onset of delirium [4-6], however, the development of drug-drug interaction may be also involved in an increased risk of adverse drug reactions (ADRs) [7-10]. In fact, older people taking five or more medications are at higher risk of delirium and falls, independent of medication indications [11].

In this paper we report the onset of delirium induced by drug-drug interaction in a previously health patient.

Case Presentation

On April 2013 an 81-year-old woman was hospitalized following a fall and the consequent lower limbs functional impotence.

History revealed the presence of heart failure, valvular and hypertensive heart disease, dyslipidemia, depression, polyarthritis and lower limb venous insufficiency treated with transdermic nitroglycerine (10 mg/day), simvastatin (10 mg/day), paroxetine (15 mg/day), allopurinol (300 mg/day), amlodipine (2.5 mg/day), losartan (50 mg/day) and acetylsalicylic acid (100 mg/day). All the drugs except that nitroglycerine were given orally. Moreover about five days before the admission she had been treated for three days with diclofenac (75 mg/day intramuscularly) for back pain propagated to lower limbs.

Brain computer tomography (CT) scan and spine magnetic resonance revealed the presence of multiple lower back herniated disks, while laboratory findings documented higher levels of cholesterol (250 mg/dL; normal range 30-200 mg/dL) and LDL (low density lipoproteins) (165 mg/dL; normal range 135-153 mg/dL) but excluded the presence of other systemic diseases. Moreover, renal and liver parameters were in normal range.

Fifteen days later the patient was discharged with diagnosis of low back pain. Due to persistent pain that impaired her quality of life and reduced her ability to walk, our patient came to a specialist in pain treatment that after clinical examination confirmed the presence of low back pain and prescribed amitriptyline (20 mg/day orally) and oxycodone/naloxone (5/2.5 mg twice/day orally).

After 15 days patient had sudden onset of hyperactive delirium with agitation, anxiety, hallucinations, severe insomnia and sleep-wake rhythm alterations. Geriatric consultation and laboratory findings excluded the presence of systemic manifestations able to induce symptoms.

Naranjo probability scale documented a probable association (score 6) between drug treatment and symptoms; amitriptyline and opioids were gradually discontinued and replaced with haloperidol (1.5 mg/day orally) and citicoline (1000 mg/day intramuscularly) with initial improvement of symptoms in about five days and with complete remission in 30 days, when the patient was able to walk again by a stick.

Concluding Remarks

In this case we report the development of delirium related to drug administration. Delirium is severe confusion that develops quickly, and often fluctuates in intensity. It is characterized by fluctuating course, attentional deficits and generalized severe disorganization of behavior.

Delirium may be caused by disease processes outside the brain, such as infections (e.g. urinary tract infection or pneumonia) or drugs, particularly anticholinergics or other depressants drugs (i.e. benzodiazepines and opiates). In our patient clinical assessment excluded the presence of systemic diseases able to induce the development of delirium, while pharmacological evaluation revealed that the patient was treated with amitriptyline and opiates for pain control able to induce delirium. Previously we reported the

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development of delirium in an elderly patient probably induced by a drug-drug interaction (DDIs) [4]. Moreover we documented that DDIs may represent a clinical problem in all patients particularly in elderly patients [6]. In the present case, the patient was treated with paroxetine that is able to induce DDIs [12]. In particular, in our case, paroxetine might have increases the plasma concentrations of opiate and antidepressant through:

a) The inhibition of the liver metabolism (via the CYP2D6 cytochrome) of opiate and antidepressant with a reduced excretion of these drugs;

b) The inhibition of P-glycoprotein with a consequent increase in opiate absorption.

However, since paroxetine inhibits CYP2D6 this effect doesn't induce relevant changes in oxycodone plasma levels [13,14].

In contrast CYP2D6 catalyses the second step of the amitriptyline metabolism, therefore its inhibition induces an increase in nortriptyline plasma levels due to the inhibition of its hydroxylation [15]. In this context, these interactions lead to an increase in plasma levels of opiate and amitriptyline with an increase in their potential adverse events.

In conclusion, we suggest that physicians thought accurately evaluate all the drugs in order to avoid the development of side effect of DDIs, particularly in elderly patients.

References

1. Alagiakrishnan K, Wiens CA (2004) An approach to drug induced delirium in the elderly. Postgrad Med J 80: 388-393.
2. Inouye SK (2004) A practical program for preventing delirium in hospitalized elderly patients. Cleve Clin J Med 71: 890-896.
3. Leentjens AF, van der Mast RC (2005) Delirium in elderly people: an update. Curr Opin Psychiatry 18: 325-330.
4. Gareri P, De Fazio P, Cotroneo A, Lacava R, Gallelli L, et al. (2007) Anticholinergic drug-induced delirium in an elderly Alzheimer's dementia patient. Arch Gerontol Geriatr 44 Suppl 1: 199-206.
5. Siniscalchi A, Gallelli L, De Fazio S, De Sarro G (2007) Psychic disturbances associated with sodium valproate plus levetiracetam. Ann Pharmacother 41: 527-528.
6. Gareri P, De Fazio P, Gallelli L, De Fazio S, Davoli A, et al. (2008) Venlafaxine-propafenone interaction resulting in hallucinations and psychomotor agitation. Ann Pharmacother 42: 434-438.
7. Gallelli L, Ferreri G, Colosimo M, Pirritano D, Guadagnino L, et al. (2002) Adverse drug reactions to antibiotics observed in two pulmonology divisions of catanzaro, Italy: a six-year retrospective study. Pharmacol Res 46: 395-400.
8. Obreli-Neto PR, Nobili A, de Oliveira Baldoni A, Guidoni CM, de Lyra Júnior DP, et al. (2012) Adverse drug reactions caused by drug-drug interactions in elderly outpatients: a prospective cohort study. Eur J Clin Pharmacol 68: 1667-1676.
9. Obreli Neto PR, Nobili A, de Lyra DP Jr, Pilger D, Guidoni CM, et al. (2012) Incidence and predictors of adverse drug reactions caused by drug-drug interactions in elderly outpatients: a prospective cohort study. J Pharm Pharm Sci 15: 332-343.
10. Marusic S, Bacic-Vrca V, Obreli Neto PR, Franic M, Erdeljic V, et al. (2013) Actual drug-drug interactions in elderly patients discharged from internal medicine clinic: a prospective observational study. Eur J Clin Pharmacol 69: 1717-1724.
11. Hubbard RE, O'Mahony MS, Woodhouse KW (2013) Medication prescribing in frail older people. Eur J Clin Pharmacol 69: 319-326.
12. Mikami A, Ohtani H, Hori S, Sawada Y (2013) Pharmacokinetic model incorporating mechanism-based inactivation of CYP2D6 can explain both non-linear kinetics and drug interactions of paroxetine. Int J Clin Pharmacol Ther 51: 374-382.
13. Grönlund J, Saari TI, Hagelberg NM, Neuvonen PJ, Laine K, et al. (2011) Effect of inhibition of cytochrome P450 enzymes 2D6 and 3A4 on the pharmacokinetics of intravenous oxycodone: a randomized, three-phase, crossover, placebo-controlled study. Clin Drug Investig 31: 143-153.
14. Kummer O, Hammann F, Moser C, Schaller O, Drewe J, et al. (2011) Effect of the inhibition of CYP3A4 or CYP2D6 on the pharmacokinetics and pharmacodynamics of oxycodone. Eur J Clin Pharmacol 67: 63-71.
15. Leucht S, Hackl HJ, Steimer W, Angersbach D, Zimmer R (2000) Effect of adjunctive paroxetine on serum levels and side-effects of tricyclic antidepressants in depressive inpatients. Psychopharmacology (Berl) 147: 378-383.